Texaphyrins vs. Texaphyrin Drug Conjugates (TDCs)

Jonathan Arambula, PhD (CEO)
Krystle Karoscik, EdD (COO)
Bobby Zahorsky (Investment Intern)

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What are Antibody Drug Conjugates?

Antibody Drug Conjugates (ADCs) have become a burgeoning market within the past few years. ADCs are composed of cytotoxic payloads covalently bonded to monoclonal antibodies (mAbs). The mAbs are designed to have a high binding affinity for antigens that are overexpressed in cancerous cells.[1] Having entered the cell, the cytotoxic payloads are severed from the mAbs and are released into the afflicted cell. These drugs then disrupt the cell through either DNA damage or microtubule disruption. In simpler terms, ADCs are made up of a scaffolding that holds an anti-cancer drug. These "scaffoldings" find their way to cancerous cells and release their contents. The result is a targeted therapy designed to be less disruptive to the body.

The Market Landscape:

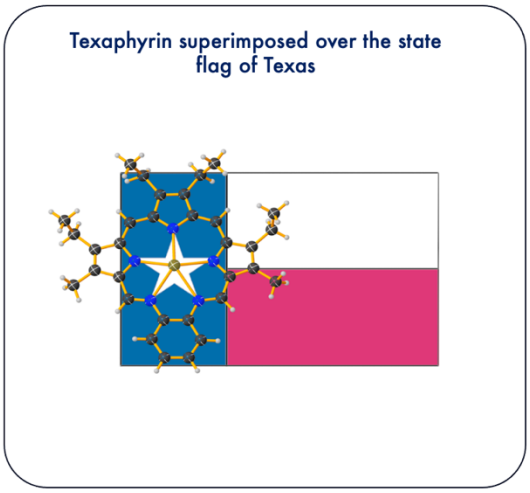
Since their first introduction in 2000 with Pfizer's Mylotarg (gemtuzumab ozogamicin), the market for ADCs has grown steadily. There are currently fourteen ADCs that have received FDA approval from large companies such as the aforementioned Pfizer, Seagan, AstraZeneca, Daiichi Sankyo, and sundry others.[2] In addition to these, one hundred new ADCs are currently in clinical trials.[3] In 2022 the Global ADC market was worth $8.6 billion and is expected to reach $23.9 billion by 2032, equating to a CAGR of 10.76%.[1]

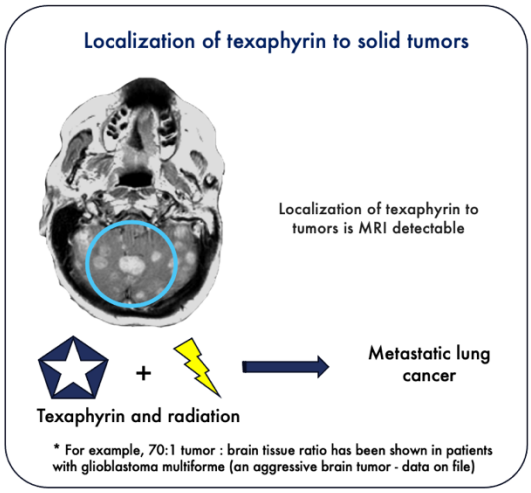
Challenges of ADCs:

While ADCs represent a large step forward in cancer treatments, significant challenges persist. One of the major challenges of ADCs is unavoidable off-target adverse events caused by a premature release of cytotoxic payloads in the body. Other known limitations include payload potency, linker instability, and insufficient targeting of the tumor microenvironment.

Why use a texaphyrin instead of an antibody?

Invented by InnovoTEX co-founder Prof. Jonathan Sessler at the University of Texas at Austin (UTA), texaphyrins were named for their chemical structure that can superimpose onto the points of the star featured on the state flag of Texas.[4–8] They were the founding technology for Dr. Sessler's first company Pharmacyclics and originally developed in combination with radiation for metastatic lung cancer.



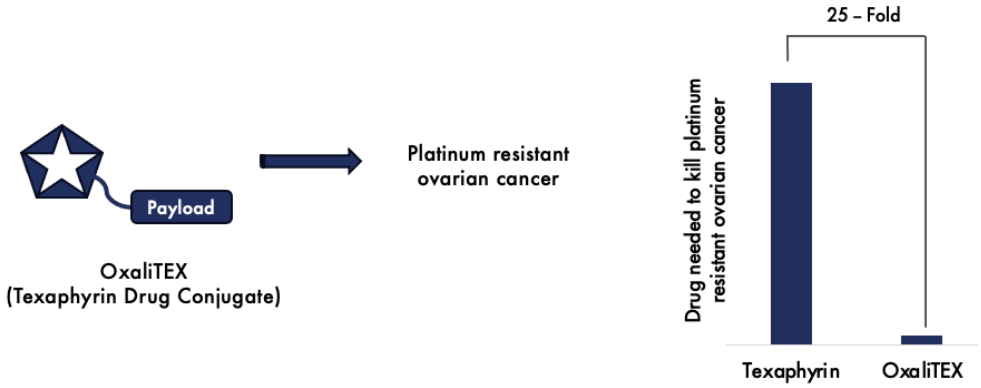


Texaphyrins significantly increased overall survival rates and met all phase III endpoints at North American based sites, but ultimately did not receive FDA approval due to differences in randomization and standard of care timelines at European sites. Patients in North America were given treatment two weeks after registering for the trial whereas European sites waited up to 10 weeks before initiating treatment. Disease progressed at some European sites and treatment responses were diminished relative to the successful outcomes at North American based sites.[9] **Some key highlights include the clinical validation of texaphyrins in over 1,000 patients to be highly selective tumor localizers and very well tolerated by patients.**[7,10–12] Following the completion of this underpowered phase III trial, all texaphyrin intellectual property and trade secrets from Pharmacyclics were transferred to UTA and are now licensed to InnovoTEX.

What makes TDCs so special?

Researchers at both UTA and MD Anderson Cancer Center began exploring ways to build off the clinical tumor localizing capabilities of texaphyrins. From this, came new chemical entities known as TDCs with the first being OxaliTEX. With InnovoTEX holding the global license to the texaphyrin and TDC intellectual property portfolio in addition to key manufacturing trade secrets, it is developing OxaliTEX as its lead clinical candidate.

OxaliTEX targets the cancer ribosome thanks to its unique anticancer payload and is being developed for 30-40% of ovarian cancers that are wild type p53 platinum resistant. In these types of cancers, OxaliTEX was found to have ~25x greater anticancer activity relative to the original texaphyrin due to its unique ability to target the cancer ribosome.[13–16]



InnovoTEX innovation:

InnovoTEX is developing a next-generation Antibody Drug Conjugate (ADC)-like platform utilizing a clinically validated tumor localizing texaphyrin core to create Texaphyrin Drug Conjugates (TDCs). These novel TDCs deliver anticancer therapies (i.e., payload) directly to the tumor. At InnovoTEX, we are using payloads that circumvent drug-resistant mechanisms.

Additional market resources:
https://ascopubs.org/doi/10.1200/EDBK_390094#:~:text=Antibody%2Ddrug%20conjugates%20(ADCs)%20are%20a%20rapidly%20emerging%20class,lethality%20of%20cytotoxic%20cellular%20poison
https://www.nature.com/articles/s41392-022-00947-7
https://www.cas.org/resources/cas-insights/drug-discovery/unveiling-potential-antibody-drug-conjugate
https://www.biospace.com/article/biopharma-industry-continues-to-bet-big-on-antibody-drug-conjugates/

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